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1: Diabetes. 1994 Jan;43(1):33-9. Related Articles, Li

Isolation of nonobese diabetic mouse T-cells that recognize nove autoantigens involved in the early events of diabetes.

Gelber C, Paborsky L, Singer S, McAteer D, Tisch R, Jolicoeur C, Buelo R, McDevitt H, Fathman CG.

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Insulin-dependent diabetes mellitus (IDDM) is thought to result from chronic cell-mediated, autoimmune islet damage. Our aim was to identify the earliest T-cell autoantigen in IDDM, reasoning that this antigen could be causally involved in the initiation of the disease. Identification of the earliest beta-cell specific autoantigen is extremely important in allowing advances in preventi and treatment of initial events in the development of inflammatory insulitis tl precedes beta-cell destruction and overt diabetes. Therefore, we analyzed the proliferative responses of peripheral T-cells from young, female nonobese diabetic (NOD) mice to extracts of pancreatic beta-cell lines. We were able t demonstrate that T-cells responsive to beta-cell antigens exist in the peripher lymphoid tissue of these mice in the absence of deliberate priming before the manifestation of histologically detectable insulitis. T-cell lines and clones isolated from the peripheral lymphatic tissues of young, unimmunized, femal NOD mice were also shown to react with extracts of beta-cells. Fractionation of the beta-cell extracts showed that these T-cell clones recognized multiple beta-cell-specific autoantigens but none of the previously reported putative autoantigens (glutamic acid decarboxylase [GAD]65, GAD67, Hsp65, insuli ICA 69, carboxypeptidase-H, and peripherin). Thus, we can conclude that th responses are specific for novel beta-cell autoantigens. Finally, NOD T-cell proliferative responses were also seen to an extract of human islets suggestin potential shared antigenic determinants between human and mouse beta-cells (ABSTRACT TRUNCATED AT 250 WORDS)

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